

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-9. **(Canceled)**

10. **(Previously Presented)** An antibody, comprising:

points of conjugation for a cytotoxic or cytostatic agent, wherein at least one point of conjugation for the cytotoxic or cytostatic agent on the antibody can be readily assigned, and wherein less than all possible points of conjugation are available for conjugation to the cytotoxic or cytostatic agent.

11. **(Previously Presented)** The antibody of claim 10, wherein the at least one readily-assignable point of conjugation is an interchain thiol, and the antibody comprises at least one interchain disulfide bond.

12. **(Canceled)**

13. **(Previously Presented)** The antibody of claim 11, wherein the antibody has four points of conjugation, and wherein the antibody has a configuration of an antibody species selected from the group consisting of species 4A, 4B, 4C, 4D, 4E and 4F of Figure 1.

14-33. **(Canceled)**

34. **(Previously Presented)** A method of reducing and conjugating a drug to an antibody resulting in selectivity in the placement of the drug, comprising:

fully reducing the antibody with a reducing agent;

treating the fully reduced antibody with limiting amounts of a reoxidizing agent to reform at least one interchain disulfide bond of the antibody, such that at least two interchain thiols remain; and

conjugating the drug to one interchain thiol.

35. **(Original)** The method of claim 34, wherein the reoxidizing agent is 5,5'-dithio-bis-2-nitrobenzoic acid, 4,4'-dithiodipyridine, 2,2'-dithiodipyridine, sodium tetrathionate or iodosobenzoic acid.

36. **(Previously Presented)** The method of claim 35, wherein the drug is a cytotoxic or cytostatic agent or an immunosuppressive agent.

37. **(Previously Presented)** The method of claim 36, wherein the cytotoxic or cytostatic agent is a minor groove binder, AEB, AEVB, MMAF, MMAE, or AFP.

38. **(Previously Presented)** The method of claim 34, wherein at least two drugs are conjugated to the antibody and each drug is conjugated to one interchain thiol.

39. **(Original)** The method of claim 34, wherein the reducing agent is DTT or TCEP.

40-42. **(Canceled)**

43. **(Previously Presented)** The method of claim 34, further comprising purifying the partially reoxidized antibody.

44-63. **(Canceled)**

64. **(Previously Presented)** A method of producing an antibody with selective conjugation of a drug comprising:

fully reducing the antibody for a period of time sufficient to produce interchain thiols, as determined by DTNB titration, by adding a large excess of a reducing agent and incubating the solution at about 37 °C for about 30 minutes;

purifying the antibody;

partially reoxidizing the antibody using an oxidizing agent to form at least one interchain disulfide bond by

cooling the reduced antibody to 0 °C;

treating the reduced and cooled antibody with 1.5 to 2.5 molar equivalents of the oxidizing agent;

mixing the solution by inversion;
allowing the solution to incubate at about 0 °C for about 10 minutes;
purifying the partially reoxidized antibody;
conjugating the drug to one interchain thiol of the partially reoxidized antibody to form a conjugated antibody; and
purifying the conjugated antibody.

65. **(Previously Presented)** The method of claim 64, wherein at least two drugs are conjugated to the antibody and each drug is conjugated to one interchain thiol.

66-73. **(Canceled)**

74. **(Previously Presented)** A method of preparing a conjugate of a protein having one or more disulfide bonds and a drug, comprising: fully reducing the protein with a reducing agent;

partially reoxidizing the protein with a reoxidizing agent; and
conjugating the drug reactive with free thiols to the protein.

75. **(Canceled)**

76. **(Previously Presented)** A partially loaded, modified protein, comprising: a binding region for interaction with a binding partner;
at least two points of conjugation having a similar accessibility or activability for conjugation of a drug or label by chemical means;

at least two drugs or labels, each drug or label covalently linked to one point of conjugation;

wherein less than all of the possible points of conjugation having a similar accessibility or activability are linked to a drug or label.

77. **(Previously Presented)** The modified protein of claim 76, wherein the protein comprises an antibody, a receptor, a receptor ligand, a hormone, or a cytokine.

78. **(Previously Presented)** The modified protein of claim 76, wherein the points of conjugation are thiol groups, amino groups, vicinal hydroxyl groups, hydroxyl groups, or carboxyl groups.

79. **(Previously Presented)** The modified protein of claim 77, wherein:
the protein is an antibody;
the binding region is an antigen-binding domain of the antibody;
the points of conjugation are thiol groups; and
the antibody comprises at least one interchain disulfide bond.

80. **(Previously Presented)** The modified protein of claim 79, wherein a thiol group is a thiol group of a cysteine residue.

81. **(Previously Presented)** The modified protein of claim 80, wherein the thiol group is a thiol group of a cysteine residue of an interchain disulfide bond.

82. **(Previously Presented)** The modified protein of claim 81, wherein each drug or label is conjugated to a thiol group of a cysteine residue of an interchain disulfide bond.

83. **(Previously Presented)** The modified protein of claim 79, wherein at least one thiol group is formed by alkylation of the epsilon amino group of a lysine residue.

84. **(Previously Presented)** The modified protein of claim 76, wherein two drugs are conjugated to the modified protein.

85. **(Previously Presented)** The modified protein of claim 79, wherein two drugs are conjugated to the modified protein.

86. **(Previously Presented)** The modified protein of claim 76, wherein the drug is a cytotoxic or cytostatic drug or an immunosuppressive agent.

87. **(Previously Presented)** The modified protein of claim 79, wherein the drug is a cytotoxic or cytostatic drug or an immunosuppressive agent.

88. **(Previously Presented)** The modified protein of claim 87, wherein the antibody comprises at least four cytotoxic or cytostatic drugs, each drug conjugated to an interchain thiol.

89. **(Previously Presented)** The modified protein of claim 79, wherein the conjugated antibody has the configuration of species 4A, 4B, 4C, 4D, 4E, or 4F of Figure 1.

90. **(Previously Presented)** The modified protein of claim 79, wherein the antibody is a humanized or chimeric antibody.

91. **(Previously Presented)** The modified protein of claim 87, wherein the drug is AEB, AEVB, MMAF, MMAE, or AFP.

92. **(Previously Presented)** A composition of modified antibodies, comprising:

at least two species of the modified antibody of claim 79, wherein the species are selected from species 4A, 4B, 4C, 4D, 4E or 4F of Figure 1.

93. **(Previously Presented)** A pharmaceutical composition comprising the modified protein of claim 76 and a pharmaceutically acceptable carrier.

94. **(Previously Presented)** A pharmaceutical composition comprising the modified protein of claim 79 and a pharmaceutically acceptable carrier.

95. **(Previously Presented)** The pharmaceutical composition of claim 94 wherein a thiol group is a thiol group of a cysteine residue.

96. **(Previously Presented)** The pharmaceutical composition of claim 95, wherein the thiol group is a thiol group of a cysteine residue of an interchain disulfide bond.

97. **(Previously Presented)** The pharmaceutical composition of claim 96, wherein each drug or label is conjugated to a thiol group of a cysteine residue of an interchain disulfide bond.

98. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein a thiol group is formed by alkylation of the epsilon amino group of a lysine residue.

99. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein two drugs are conjugated to the modified protein.

100. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein the drug is a cytotoxic or cytostatic drug or an immunosuppressive agent.

101. **(Previously Presented)** The pharmaceutical composition of claim 100, wherein the antibody comprises at least four cytotoxic or cytostatic drugs, each drug conjugated to an interchain thiol.

102. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein the conjugated antibody has the configuration of species 4A or 4B, 4C or 4D, 4E, or 4F of Figure 1.

103. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein the antibody is a humanized or chimeric antibody.

104. **(Previously Presented)** The pharmaceutical composition of claim 100, wherein the drug is AEB, AEVB, MMAF, MMAE, or AFP.

105. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein there is an average of 4 drugs per antibody.

106. **(Previously Presented)** The pharmaceutical composition of claim 94, wherein there is an average of 2 drugs per antibody.

107. **(Previously Presented)** A method for the treatment of cancer, immune disease, autoimmune disease or infectious disease in a patient, comprising administering to the patient an amount of the modified protein of claim 10.

108. **(Previously Presented)** A method for the treatment of cancer, immune disease, autoimmune disease or infectious disease in a patient, comprising administering to the patient an amount of the modified protein of claim 76.

109. **(Previously Presented)** The method of claim 108 wherein:
the protein is an antibody;

the binding region is an antigen-binding domain of the antibody;
the points of conjugation are thiol groups; and
the antibody comprises at least one interchain disulfide bond.

110. **(Previously Presented)** A method for the treatment of cancer, immune disease, autoimmune disease or infectious disease in a patient, comprising administering to the patient an amount of the pharmaceutical composition of claim 93.

111. **(Previously Presented)** The method of claim 110 wherein;
the protein is an antibody;
the binding region is an antigen-binding domain of the antibody;
the points of conjugation are thiol groups; and
the antibody comprises at least one interchain disulfide bond.

112. **(Previously Presented)** The method of claim 75, wherein at least two drugs are conjugated to the antibody and each drug is conjugated to one interchain thiol.